Synthetic Organic Chemicals

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The Story of Ergosterol

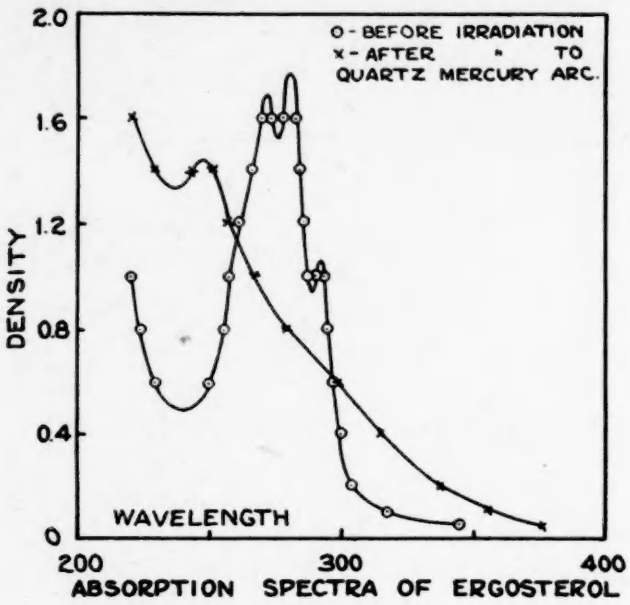
ONE of the most pathetic sights in the world is a child with an acute case of rickets; the deformed bones and the tired, old expression of a six months old baby will never be forgotten by anybody who has seen such a case. Rickets is no new disease; the skeletons in the tombs of all ages show that man has always suffered from it, but its origin only began to become clear when Mellanby classified it definitely as due to a deficiency in diet, the material which was lacking being named by him the antirachitic vitamin.

We know now that the antirachitic vitamin or Vitamin D occurs in conjunction with fats, by far the richest source being cod liver oil, and it was soon found that the feeding of cod liver oil to rachitic children would at once increase the deposition of calcium on the bones and if continued cure the rickets.

A clinician, Palm, in 1890, associated the incidence of rickets with deficiency of sunlight. Buchholz, in 1905, cured 16 cases of rickets with light from artificial sources. Huldschinsky, in 1919, gave the first convincing proof (with x-ray findings) of the effect of mercury vapor quartz lamp on the bones of 4 children with advanced rickets. Hess and Unger, in 1921, were the first to prove the truth of Palm's observation, i. e., that rickets in children could be cured by sunlight alone. Their work was confirmed by Park and McCollum, working on rickets in the rat. The active rays in sunlight were found to be the extreme limit of the ultra-violet which reaches us. While the sun presumably emits rays of all wave-lengths, there is in the higher atmosphere a quantity of ozone, perhaps formed from the oxygen by the short ultra-violet waves, which absorbs all the ultra-violet of wave-length lower than about 300 mμ, and Hess found that it was these short waves between 300 and 320 which are effective in curing rickets. Light sources containing larger amounts of the ultra-violet and especially light sources rich in the region between 270 and 290 mμ are very much more effective in curing rickets, so that exposure to a mercury quartz lamp for a few minutes is equivalent to hours of exposure to sunlight, and treatment with electric arcs became a recognized method of dealing with the disease.

Then Steenbock, working at the University of Wisconsin, and Hess and Weinstock found that a rickets-producing diet could be made protective by exposure to ultra-violet light; also, that the sterol fraction of the diet was the part that became activated; and that "chemically pure" cholesterol could be made antirachitic after exposure to light. Then

Rosenheim in England and Hess and Windaus in this country found that cholesterol, which had been purified by regeneration from the dibromide, did not have any curative effect after exposure to ultra-violet light, but that many samples of cholesterol contained a trace of another sterol, which was identical with the ergosterol isolated by Tanret from ergot, a black fungus which grows on the rye plant.



ABSORPTION SPECTRA OF ERGOSTEROL

Ergosterol is distinguished by a peculiar absorption spectrum, illustrated in the figure, and when a solution is exposed to ultra-violet light, this absorption band vanishes and a new absorption band further in the ultra-violet appears. Irradiated ergosterol has proved on test to be extraordinarily effective in curing rickets. Rats which had been fed on a Vitamin D free diet so that they developed acute rickets have been cured by as little as 1/10,000th of a milligram of irradiated ergosterol per day. The curative dose of the so-called "pure" cholesterol was 1 mg. per rat per day, so from this the smallest of the dose of the pure material is evident.

The matter was brought to our attention by some experiments which were conducted at the Medical School of the University of Rochester, and when Rosenheim's paper appeared, we were asked to isolate ergosterol in the pure state.

The best source for ergosterol, when relatively small quantities are required for experimental work, appears to be ergot, since this seems to contain no cholesterol, the separation of which from the ergosterol is so difficult as to be impracticable. On the other hand, as shown by Tanret, the ergosterol in ergot is accompanied by a small proportion of a sterol called "fungisterol" which is apparently a lower homologue of cholesterol. This is somewhat more soluble in organic liquids than ergosterol and can be removed by fractional crystallization. The amount of ergosterol isolated by Tanret was approximately 100 mg. per kilo of ergot; we have found that this yield can be increased by about 50% by employing methods designed to secure the whole of the unsaponifiable matter present in the fatty constitutents.

Since the world's supply of ergot is limited, it is probable that the manufacture of ergosterol in a commercial way, if undertaken, will have to employ as raw material yeast or some similar product which can be produced in unrestricted quantities.

Hints on Filtration in Organic Preparations

IN organic preparative work by far the majority of filtration operations are carried out with the aid of suction. When only small amounts of material are in treatment, filtration of recrystallization solutions may be advantageously effected with folded papers, but for volumes of a liter or more the use of suction will generally be found preferable. In such a case the funnel should be warmed before use; this is conveniently done by attaching it in the usual way to a filtering flask and passing steam into it from below. A rapid current of air is sufficient

to dry it while still warm. Or the funnel may be warmed by stoppering it to a flask in which the appropriate solvent is vigorously boiling.

Crystals are always collected in a suction funnel, fitted with a hardened paper from which the product can be removed without danger of contamination with cellulose fibers. For small amounts—particularly when relatively large volumes of mother liquor are present—the conical Hirsch suction funnel is preferable to the Büchner type.

Suction funnels of all laboratory varieties possess stems which are too short for convenient use with conical suction flasks, the filtrate often having an annoying tendency to froth or splash from the funnel into the sidearm. This defect may be remedied by attaching to the stem of the funnel a wide rubber tube long enough to discharge the filtrate well below the level of the side tube.

A preferable alternative is to replace the customary filtration flask by a stout, wide-mouthed bottle or, even better, a round-bottomed flask. Suction is applied through a right-angled tube inserted in the stopper attaching the funnel. This scheme works satisfactorily with Pyrex flasks of from three to twelve liters capacity, and with funnels up to about fifteen centimeters in diameter. For larger apparatus it is advisable to support the funnel on a tripod and to connect it by means of a suitable adapter (stoppered to the stem of the funnel) and glass tubing joined with pressure tube to the receiving flask.

When very large quantities are to be filtered, a different and highly unorthodox method may be found useful. The funnel is fitted with an adapter to which is attached a pressure tube leading to the receiving flask. The filter paper is moistened and placed in position, and suction applied. The funnel is then allowed to hang upside down in the mixture to be filtered; it may either be lowered gradually so as first to draw off the supernatant liquid or at once placed near the bottom of the container, so that the solids collect around it and form their own filtering mat. In the latter case, which is especially applicable to the case of readily filterable mixtures containing large bulks of solid, the filter-cake can be washed without removing the funnel.

Slimy solids, which first pass the filter and then clog it, cannot be satisfactorily collected with suction. The ordinary conical paper filter of the inorganic chemist is less efficient than a flat filter paper laid on a Büchner funnel: as soon as the filtrate comes through clear, the first runnings are returned to the funnel and the filtration is carried out entirely by gravity. The cake can then be washed in the same way.

The use of a thin rubber sheet for pressing out finely divided solids, as recommended by Gortner, is often of great value. It is especially applicable in the case of precipitates which tend to "channel" or crack when approaching dryness.

Large quantities of mixtures to be filtered are conveniently transferred from container to filter by means of a cup and saucer of heavy china. The saucer is employed to prevent material from dropping from the cup during transference and to keep the cup from contact with laboratory table.

We are always glad to receive comments and suggestions from readers; have you any to make?

Organic Chemicals as Analytical Reagents

III REAGENTS FOR NICKEL

α–BENZIL DIOXIME

Atack, Analyst, *38*, 316 (1913)

In alcoholic solution, α-benzil dioxime gives a bright red precipitate with nickel salts. The solution to be analyzed should contain less than 0.025 gm. Ni and should be made slightly ammoniacal. A slight excess of the warmed reagent is added with stirring, and the precipitate coagulated by heating on a water bath. The precipitate is washed with warm 50% alcohol, then hot water and finally dried at 110° C. It contains 10.93% nickel. Nitrates must be destroyed in the original sample by evaporation with sulphuric acid.

DICYANDIAMIDINE SULPHATE

Grossmann and Schück, Chem. Zeit. *31*, 335,911 (1907)

This reagent in alcoholic solution precipitates nickel in the form of a yellow orange organic compound. The nickel solution is made slightly ammoniacal and 10-20 cc. of 10% dicyandiamidine sulphate is added. A slight excess of 10% potassium hydroxide is added and the precipitate is allowed to stand over night. After washing and drying at 115° the precipitate contains 22.5% Ni. Copper salts give a brown precipitate under the same conditions so that this metal must be removed previous to the nickel determination.

DIMETHYLGLYOXIME

Weeldenburg, Chem. Weekblad, *21*, 358 (1924)

This reagent may be used in alcoholic or aqueous sodium hydroxide solution. Ores or alloys are dissolved in aqua regia, lead and the alkaline earths precipitated with ammonium sulphate, and the filtrate then treated with hydrogen sulphide. Nickel glyoxime is precipitated by adding the reagent to the filtrate after the addition of tartaric acid and ammonium chloride. (See also "Technical Methods of Analysis," Griffin: McGraw Hill.)

POTASSIUM DITHIO-OXALATE

Fairhall, J. Ind. Hyg. *8*, 528 (1926)

A colorimetric method for the determination of nickel in tissues, excreta, foodstuffs, etc., is based on the formation of magenta-colored nickel dithio-oxalate. As small amounts as one milligram can be determined with an accuracy of 1%. Iron must be removed, but the presence of alkali and alkali earth cations in small amounts does no harm.

New Chemicals

The following preparations have been added to our list since the last issue of this pamphlet:

* 4-Acetamino-1.3-dimethylbenzene
* 1-Amino-2-naphthol Hydrochloride
* 2-Bromopentane
* Cellulose Triacetate
Crotonaldehyde (Practical)
* 2.6-Dibromo-4-aminophenol
* 2.6-Dibromoquinonechloroimide
* p-Diethylaminobenzaldehyde
Hexamethylethane
Mesityl Oxide (Technical)
* 5-Nitro-4-acetamino-1.3-dimethylbenzene
* n-Pentane (Synthetic)
* Phenylglucosazone
Phytin (Technical)
Sulfanilic Acid (Technical)
Trimethylacetic Acid
* p-Xylyl Acetate (Technical)
* p-Xylyl Bromide (Technical)

* *Made or purified in the Kodak Research Laboratories.*